DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

Rec'd 3.26.2010

SENT VIA TELEFAX

Docket No. FDA-2010-N-0134

Dear ANDA Applicants:

This letter addresses whether the March 4, 2009 expiration of U.S. Patent No. 5,608,075 ('075 patent) affects the first applicant's eligibility for 180-day exclusivity for generic versions of Merck's Cozaar and Hyzaar drug products, and supplements the March 11, 2010 letter to ANDA applicants that was posted at www.regulations.gov in Docket No. FDA-2010-N-0134. As explained below, in light of the Court of Appeals' decision in Teva Pharms., USA, Inc. v. Sebelius, No. 09-5281 (D.C. Cir. Mar. 2, 2010) ("Teva slip op."), we have concluded that the expiration of the '075 patent does not result in a forfeiture of the first applicant's eligibility for exclusivity for ANDAs referencing Cozaar and Hyzaar.

Background

FDA has pending before it ANDAs referencing Cozaar (losartan potassium) Tablets and Hyzaar (losartan potassium and hydrochlorothiazide) Tablets. Among the patents submitted to FDA for Cozaar and Hyzaar, and thus relevant to the approval date for these ANDAs, is the '075 patent. FDA's Orange Book shows that the '075 patent was submitted by Merck, and that Merck later requested delisting of the patent. Merck has also recently informed FDA that the expiration date for the '075 patent should be revised from March 4, 2014, to March 4, 2009.[1] The Orange Book currently displays the March 4, 2009 expiration date for the '075 patent.

The timing of approval of ANDAs referencing Cozaar and Hyzaar will be affected by, among other things, any 180-day exclusivity under section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act (the Act) available to a first applicant to challenge the '075 patent.[2] Under the Act, as amended by the MMA, a 180-day exclusivity period will not delay approval of any ANDA referencing Cozaar or Hyzaar if the exclusivity has been forfeited by the first applicant. See section 505(j)(5)(D)(i). The delisting of the '075 patent by Merck and the March 4, 2009 patent expiration date implicate two distinct 180-day exclusivity forfeiture provisions in the Act, sections 505(j)(5)(D)(i)(I) and (VI), respectively.

[1] Apotex notified FDA on March 9, 2010, that records of the U.S. Patent and Trademark Office (PTO) showed that the '075 patent had expired no later than March 30, 2009, due to non-payment of fees. Pursuant to the procedure described in 21 C.F.R. § 314.53(f), FDA sought information from Merck regarding the correct expiration date for the '075 patent. By letters of March 12, 2010, Merck stated that the correct expiration date for the '075 patent is March 4, 2009.

[2] The 180-day exclusivity for ANDAs referencing Cozaar and Hyzaar is governed by section 505(j)(5)(B)(iv) and related provisions, as modified by the Access to Affordable Pharmaceuticals provisions of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (Dec. 8, 2003) (the MMA).

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Delisting of the '075 Patent

The U.S. Court of Appeals for the D.C. Circuit recently considered the effect of the delisting of the '075 patent on a first applicant's claim to 180-day exclusivity arising from a paragraph IV certification to that patent. Teva slip op. The court reviewed the delisting provision, section 505(j)(5)(D)(i)(I)(bb)(CC). The Agency had applied this provision in previous adjudications such that delisting of the patent for any reason by the NDA holder could result in forfeiture. Teva had asserted that FDA's interpretation of the delisting provision, although applied by FDA only in adjudications involving other drugs and different parties, was both subject to immediate review by the court and not supported by the statute.[3] The court, in a 2-1 decision, agreed with Teva on both grounds, and ruled that Merck's delisting of the '075 patent could not be the basis for forfeiture of exclusivity by the first applicant for generic Cozaar and Hyzaar. Slip op. at 29.

The D.C. Circuit, in response to a request from Teva, issued the mandate on an expedited basis on March 12, 2010, and remanded the case to the district court.[4] On March 26, 2010, the district court amended an order it had issued on March 16, 2010, to clarify that Teva has not forfeited its 180-day exclusivity under the Failure to Market provision, section 505(j)(5)(D)(i)(I). The district court stated that forfeiture due to patent expiration under section 505(j)(5)(D)(i)(VI) was not raised in Teva's Complaint and was not addressed by the D.C. Circuit in either its March 2, 2010 Opinion or in the March 12, 2010 issuance of the mandate. The district court ordered FDA to file a notice of its decision on the '075 patent expiration issue by 5 p.m. on March 26, 2010.

Expiration of the '075 Patent

When Teva first raised the question of 180-day exclusivity for ANDAs referencing Cozaar and Hyzaar before the district court in June 2009, FDA's records showed a March 4, 2014 expiration date for the '075 patent, and no outside party had brought any other expiration date for the patent to the Agency's attention. It was only after the March 2, 2010 Teva decision that FDA was notified by Apotex that the Patent and Trademark Office records showed that the '075 patent had expired for failure to pay fees. Now that Merck has confirmed to FDA that the '075 patent expired on March 4, 2009, FDA is addressing whether the patent expiration is a separate basis, apart from the delisting, for forfeiture of exclusivity.[5] To obtain comment from interested parties on the effect of the revised patent expiration date, FDA sent a letter to ANDA applicants on March 11, 2010, and opened a public docket for submission of comments (FDA-2010-N-0134).

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[3] On July 31, 2009, the U.S. District Court for the District of Columbia found that it had jurisdiction to review the matter, but granted judgment in favor of the government on the merits. Teva Pharms. USA, Inc. v. Sebelius, 638 F. Supp. 2d 42 (D.D.C. 2009).

[4] The Solicitor General is considering seeking rehearing of the Court of Appeals' decision. If rehearing is sought by the government and granted, the mandate would be recalled.

[5] In Teva, the government argued that the court should not address the dispute concerning 180-day exclusivity being pressed by plaintiff Teva until FDA had decided that issue. One basis for the government's position was the potential that factual and/or legal issues specific to the circumstances associated with the Teva claim would require an FDA analysis that would, at a minimum, be useful to the court in its decision-making. The court rejected that position. FDA believes that the new and complicated issues raised by the expiration of the patent at issue in this case provide a good example of why courts should await an agency decision in a particular matter rather than anticipate an agency's decision based on previous rulings in similar matters.

FDA has considered these submissions, as well as the relevant statutory provisions, regulations, and case law, in developing the views described in this response.[6]

Neither the district court nor the D.C. Circuit addressed the effect of the expiration of the '075 patent on the first applicant's eligibility for 180-day exclusivity, nor could they have done so because, as noted, when the courts ruled, neither they nor FDA was aware of the fact that the '075 patent had expired. Therefore, FDA is addressing the matter here. First, the Agency analyzes the issue as if it were writing on a clean slate, and interpreting and applying the statute without reference to the recent Teva decision. Second, the Agency describes the effect of the Court of Appeals' reasoning in the Teva delisting decision on the outcome in this particular patent expiration matter.

Merck, the NDA holder, has notified FDA that the sole patent giving rise to a claim of 180-day exclusivity for ANDAs referencing Cozaar and Hyzaar, the '075 patent, has expired. The patent information provided to FDA by the NDA holder controls for patent certification purposes. Teva Pharms., USA, Inc. v. Leavitt, 548 F.3d 103, 106 (D.C. Cir. 2008) ("FDA operates in a purely ministerial role, relying on NDA holders to provide the Agency with accurate patent information."). Therefore, in assessing the first applicant's claim to exclusivity, FDA will rely on Merck's statement that the '075 patent has expired.

The effect of a patent expiration on exclusivity is specifically addressed in the 180-day exclusivity provisions applicable to the ANDAs referencing Cozaar and Hyzaar. Section 505(j)(5)(B)(iv) of the Act, as amended by the MMA, states:

> Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

"Subparagraph (D)" describes how a first applicant will forfeit its 180-day exclusivity period upon the occurrence of different types of a "forfeiture event" with respect to that applicant. Section 505(j)(5)(D). Among the defined events resulting in forfeiture is "Expiration of All Patents," which occurs when "[a]ll of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired." Section 505(j)(5)(D)(i)(VI). If this forfeiture event applies to a first applicant, the applicant forfeits exclusivity immediately upon the expiration of all patents as to which it qualified as a first

[6] Due to the limited amount of time remaining before April 6, 2010, when one or more ANDAs referencing Cozaar and Hyzaar are expected to be eligible for final approval, FDA initiated its request for comment on the effect of a March 4, 2009 expiration date for the '075 patent before it had received the confirmation from Merck of the correct expiration date. Further, because of the exceptional circumstances of this case, FDA is making a decision on 180-day exclusivity before April 6, 2010. Because of the possibility that relevant facts will change, it is FDA's usual practice to wait until at least one ANDA is otherwise eligible for final approval before the Agency makes decisions regarding 180-day exclusivity. Among other considerations underlying FDA's decision to address the patent expiration at this time is the Teva court's decision on 180-day exclusivity based on events involving the same patent at issue in the current matter.

applicant.[7] If there is only one patent that serves as a basis for 180-day exclusivity, when that patent expires, there will be no exclusivity for the drug product, and the Agency may approve any otherwise approvable ANDA.

Under FDA's longstanding interpretation, once a patent expires, eligibility for 180-day exclusivity based on that patent is extinguished. This is true under both the pre-MMA 180-day exclusivity provisions and the MMA exclusivity provisions applicable to the ANDAs referencing Cozaar and Hyzaar. The pre-MMA exclusivity provisions did not explicitly address whether 180-day exclusivity could survive the expiration of the patent. In addressing that statutory gap, FDA stated that once a patent expires, the correct certification to the patent is a "paragraph II" certification pursuant to section 505(j)(2)(A)(vii)(II)("that such patent has expired"). Once the application no longer contains a paragraph IV certification to the patent, the applicant no longer has a basis to obtain exclusivity as to that patent. This was held to be a reasonable interpretation of the pre-MMA exclusivity provision. Dr. Reddy's Labs., Inc. v. Thompson, 302 F. Supp. 2d 340, 356-57 (D.N.J. 2003). Moreover, even when the D.C. Circuit found in Ranbaxy Labs. Ltd. v. Leavitt, 469 F.3d 120 (D.C. Cir. 2006), that the pre-MMA exclusivity provisions would not permit an NDA holder's delisting of a patent to defeat a first applicant's claim on exclusivity, the court noted that "as Ranbaxy and Teva acknowledged at oral argument, the text and the structure of the [pre-MMA] statute suggest a distinction between expiration and delisting such that the first generic applicant may no longer retain exclusivity when the patent has expired." Id. at 126 n.3 (citing, inter alia, Dr. Reddy's Labs.). The forfeiture provision at section 505(j)(5)(D)(i)(VI), enacted in the MMA, thus embodies the familiar principle that 180-day exclusivity does not survive patent expiration.[8]

The issue presented by the expiration of the '075 patent is not whether, as a general rule, exclusivity will be forfeited pursuant to section 505(j)(5)(D)(i)(VI) upon the expiration of a patent, but whether a patent expiration for failure to pay fees is an exception to this rule.[9] The

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[7] The forfeiture events described in sections 505(j)(5)(D)(i)(II)-(V) are similarly immediate in effect if they are found to apply to a first applicant. It is interesting to note the contrast between these "immediate" forfeiture events, which provide no opportunity for the first applicant to use its exclusivity period once the forfeiture event has occurred, and the "Failure to Market" forfeiture event described in 505(j)(5)(D)(i)(I), which provides that upon the occurrence of certain events, rather than face immediate forfeiture, the first applicant will have the opportunity to begin commercial marketing of the drug product and thus start the running of its 180-day exclusivity period. For each of the events set out in 505(j)(5)(D)(i)(I)(bb), the first applicant has 75 days from the date of the specified event to begin marketing and receive the benefits of exclusivity. These provisions describe events that could occur with respect to "the first applicant *or any other applicant*" (emphasis added), as well as the patent delisting provision interpreted by the court in Teva. Presumably, Congress structured this exclusivity forfeiture provision so that, even if it is an applicant other than a first applicant that triggers a forfeiture by, for example, obtaining a final decision of non-infringement, the first applicant will nevertheless have a limited opportunity to benefit from being the first to challenge the patent. It is reasonable for FDA to conclude that, once at least one applicant has obtained a final court decision or settlement stating that the patent at issue is invalid or not infringed - or the patent has been delisted by the NDA holder because it does not meet the patent listing requirements - Congress sought to balance the benefits derived from the exclusivity incentive against the delay in the availability of generic drugs resulting from that exclusivity, and thus established a limit on the length of time during which the exclusivity would be available. In the case of patent expiration, Congress concluded that not even a limited 180-day exclusivity barrier to approval was warranted once the patent expired.

[8] The MMA did not revise the descriptions of patent certifications set forth at section 505(j)(2)(A)(vii).

[9] Teva, for example, appears to acknowledge that forfeiture will occur upon "natural patent expiry." March 18, 2010 Comment from Teva at 3.

Agency's view is that, if it were writing on a clean slate, it would interpret the statute so that patent expiration for any reason is a patent expiration forfeiture event. FDA believes that interpretation is most consistent with the plain meaning of the words of the statute and with a workable and appropriate approach to administration of the statute.

The text of the patent expiration forfeiture event provision does not provide a basis to distinguish between "natural patent expiry" and expiration for some other reason.[10] Section 505(j)(5)(D)(i)(VI) refers broadly to forfeiture when "all of the patents ... have expired." There is no language qualifying the type of expiration the Agency is to consider relevant for forfeiture.[11] Thus, there is no apparent statutory basis for the Agency to conclude that only some patent expirations result in forfeiture.

Some of the comments noted a number of reasons why FDA should create an exception to patent expiration forfeiture when the patent expires because the patent owner has failed to pay applicable fees. Among these are concerns about the lack of certainty regarding the expiration when the patent expires due to non-payment of fees. The March 18, 2010 comments from Teva and from Olsson, Frank & Weeda (OFW) identify situations in which a patent that has expired can be "revived" through payment by the patent owner of fees. Teva comment at 2-3; OFW comment at 3-4, 9-10.

Although it may well be the case that a patent that has expired for failure to pay fees could, in certain circumstances, be revived, this possibility alone is an inadequate basis to maintain that a later expiration date must control. As an initial matter, FDA will not change the applicable patent expiration date unless the NDA holder tells the Agency to do so. If the NDA holder (who is also likely to be the patent owner or licensee) notifies FDA that the patent has expired due to failure to pay fees, it can be presumed to have resolved at least to a reasonable certainty the finality of the patent expiration. Further, the concerns about uncertainty of expiration would presumably extend to all situations in which a patent has expired due to failure to pay fees, including those in which, although 180-day exclusivity is not an issue, reliance on a later expiration date could delay generic drug approvals. For example, if an NDA holder notified FDA that a patent on a drug as to which no ANDA had yet been submitted had expired due to failure to pay fees, but FDA refused to accept the NDA holder's representation because of uncertainty that the patent would remain "expired," future ANDA applicants would be required to submit patent certifications for a patent that may have its natural patent expiration years in the future. If the NDA holder is sufficiently certain its patent has expired that it notifies FDA of that fact, FDA believes that generic drug applicants are entitled to rely on that patent expiration date in seeking approval for their drug products.

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[10] Teva's comment does not define "natural patent expiry." For example, that term presumably could encompass both the expiration of the original 17 or 20 year term of a patent and the expiration of the term of certain patent claims that have been extended under 35 U.S.C. § 156. FDA's requirements do not limit the type of patent expiration information that may be submitted to FDA. 21 C.F.R. § 314.53.

[11] Based on the lengthy list of patents that expired on March 4, 2009, that was submitted as Attachment B to the March 9, 2010 Apotex letter raising the '075 patent expiration issue, expiration for failure to pay fees is not uncommon. Nonetheless, FDA is not aware of any other case in which it has been notified by an NDA holder that a patent that had been submitted to FDA and listed in the Orange Book has expired due to non-payment of fees.

Finally, in assessing what expiration date should control for purposes of 180-day exclusivity, it is appropriate for FDA to continue to rely on the NDA holder's representations to FDA. Teva v. Leavitt, 548 F.3d at 106. In this case, for example, although Apotex brought the question of the correct expiration date for the '075 patent to FDA's attention, the Agency did not consider the patent expiration date to be March 4, 2009 (and publish that date in the Orange Book) until Merck notified FDA that March 4, 2009 was the correct date. Had Merck maintained that the patent expiration date remained March 4, 2014, FDA would have retained the March 4, 2014 date in its records and relied on that date for patent certification, exclusivity, and application approval purposes. As stated in FDA's regulations,

> Unless the application holder withdraws or amends its patent information in response to FDA's request, the agency will not change the patent information in the list [the Orange Book]. If the new drug application holder does not change the patent information submitted to FDA, ... an abbreviated new drug application under section 505(j) of the act submitted for a drug that is claimed by a patent for which information has been submitted must, despite any disagreement as to the correctness of the patent information, contain an appropriate certification for each listed patent.

21 C.F.R. § 314.53(f). Even though information on patent expirations due to failure to pay fees is available from the PTO, it would not be an appropriate use of FDA resources for FDA to forgo its ministerial role in these matters and make its own assessments of patent expiration. In light of the commenters' concerns about the uncertain nature of these patent expirations, it would seem particularly important that the Agency continue to defer to the NDA holder's judgment regarding the expiration of its patent.

The expiration of a patent is a specific basis for forfeiture of exclusivity under the MMA, and it also necessitates a change in the ANDA applicants' patent certifications. The MMA patent certification provisions, like the pre-MMA provisions, state that the appropriate certification to an expired patent is a "paragraph II" (that such patent has expired). Section 505(j)(2)(A)(vii)(II). Upon expiration of a patent, a paragraph IV certification to the patent automatically becomes invalid. Ranbaxy Labs Ltd. v. FDA 96 Fed. Appx. 1 (D.C. Cir. 2004) (unpublished). Thus, a paragraph IV certification to the expired '075 patent is invalid, and the appropriate certification to the patent is "paragraph II." The 180-day exclusivity provision at section 505(j)(5)(B)(iv) directs that FDA determine whether an ANDA "contains a [paragraph IV] certification ... and is for a drug for which a first applicant has submitted an application containing such a certification." When a first applicant's ANDA does not contain a valid paragraph IV certification or a non-first applicant's ANDA no longer contains a paragraph IV certification, the 180-day exclusivity provision at section 505(j)(5)(B)(iv), by its own terms, does not apply.[12] Thus, permitting the first applicant to retain exclusivity as to an expired patent requires FDA to take an action that is not sanctioned by the words of the statute.

[12] The MMA also defines a "first applicant" eligible for exclusivity as an applicant that, among other things "submits a substantially complete application that contains *and lawfully maintains* [a paragraph IV certification]." Section 505(j)(5)(B)(iv)(II)(bb) (emphasis added). An applicant cannot lawfully maintain a paragraph IV certification to a patent that has expired.

For the reasons described above, FDA concludes that if it were assessing this issue without reference to the Teva decision, it would find that, under the plain language of the statute, because the '075 patent will have expired by the time any ANDA referencing Cozaar or Hyzaar is ready for approval, any first applicant previously eligible for 180-day exclusivity as to the '075 patent forfeits that exclusivity. Moreover, even if the statutory language is considered ambiguous, FDA concludes loss of exclusivity under these circumstances is most consistent with the statute's text and goals, and provides the most reasonable way of administering the statute.

Effect of Teva Decision on Patent Expiration Forfeiture

FDA does not believe it can assess the effect of expiration of the '075 patent due to nonpayment of fees on exclusivity for generic Cozaar and Hyzaar without consideration of the D.C. Circuit's Teva decision and the reasoning in that decision regarding the delisting of the '075 patent.

In Teva, the D.C. Circuit concluded that Teva is entitled to exclusivity, in spite of the fact that the NDA holder has requested delisting of the patent, based on the "structure" of the statute, regardless of the words of the statute.[13] Moreover, the court concluded that this analysis was appropriately considered under "Chevron step one," i.e., that there was no statutory ambiguity that FDA is free to resolve based on its understanding of the statute and the industry it regulates. Slip op. at 29. After rejecting Teva's "linguistic" argument, slip op. at 24, the court adopted a "structural argument" based on the pre-MMA Ranbaxy case. Slip op. at 24. It found that the structure of the MMA exclusivity provisions, as with the pre-MMA exclusivity provision considered in Ranbaxy, does not permit an NDA holder to "unilaterally" deprive the generic applicant of its exclusivity on the basis of delisting.[14] Slip op. at 5, 29. This reasoning thus appears to preclude a forfeiture of exclusivity on the basis of a patent expiration where the expiration is in the control of the NDA holder. Because the '075 patent expired due to Merck's

[13] The D.C. Circuit specifically stated:

> We see nothing in the 2003 amendments to the Food, Drug, and Cosmetic Act that changes the structure of the statute such that brand companies should be newly able to delist challenged patents, thereby triggering a forfeiture event that deprives generic companies of the period of marketing exclusivity they otherwise deserve. For that reason, the interpretation of the statute that the FDA has adopted in two recent adjudications, and that it regards itself as bound by law to apply to Teva's ANDAs for losartan products, fails at Chevron step one.

Slip op. at 29.

[14] The Teva court's decision suggests that it believed the statute would permit innovator companies to delist patents at will to deprive the first applicant of exclusivity, i.e., that "Brand manufacturers are . . . free to delist challenged patents whenever they please ...." Slip op. at 24, 25. Patent listing is not optional. In fact, NDA holders are required by statute to provide patent information to FDA if, but only if, the patent claims the drug product or an approved use of the product, and if "a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." Section 505(b)(1). Thus, the patent holder may not simply withdraw or change patent information previously submitted to FDA because of some desire to interfere with the 180-day exclusivity of a potential generic competitor. It is, of course, true that FDA does not have the patent expertise to enforce the statutory requirement that appropriate patents be listed or delisted. Because the continued listing of an inappropriate patent, with the resulting blocking of competition, can place the NDA holder in jeopardy of antitrust damages, considerations of antitrust liability may well be factors in innovator decisions to withdraw patent information previously submitted. In fact, settlement of disputes between innovator companies and the Federal Trade Commission can result in patent delistings. See, e.g., Report, In the Matter of Bristol-Myers Squibb Co., Docket No. C-4076 (Federal Trade Comm'n, June 20, 2003) (describing delisting of patents for Serzone, Buspar, and Taxol). The Teva decision could affect the availability and effectiveness of delisting as a remedy.

failure to pay applicable fees, that expiration, consistent with the Court of Appeals' reasoning in Teva, is not a grounds for forfeiture of the first applicant's exclusivity. Although FDA believes this result is inconsistent with the plain language of the statute, as discussed above, it believes it is appropriate to apply the Court of Appeals' reasoning to the present facts. In the event the D.C. Circuit reconsiders and revises the decision in Teva, FDA reserves the right to revisit these conclusions regarding 180-day exclusivity for ANDAs referencing Cozaar and Hyzaar.

FDA thus finds that, consistent with the reasoning of the Court of Appeals, despite having been delisted by the patent owner and having expired, the '075 patent nevertheless must be considered to remain a basis for 180-day exclusivity. FDA will not approve any other ANDA referencing Cozaar or Hyzaar until the first applicant has received approval of its ANDA, begun commercial marketing, and the 180-day exclusivity period has expired.[15] The Agency makes this finding even though it is not the result that FDA, as the agency that administers the statute, believes is appropriate given the relevant statutory language or the policies underlying the statute.

Conclusion

For the reasons described above, the Agency has concluded that, in light of the D.C. Circuit's decision in Teva, the March 4, 2009 expiration of the '075 patent for failure to pay applicable fees does not result in forfeiture of the first applicant's 180-day exclusivity for ANDAs referencing Cozaar and Hyzaar. If you have any questions regarding this decision, please contact Dave Read, Regulatory Counsel, Office of Generic Drugs at (240) 276-9310.

Sincerely,

{See appended electronic signature page}

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

[15] We note that even though the Teva litigation has proceeded on the assumption that a first applicant will receive approval and begin marketing promptly after all applicable patent and exclusivity barriers expire, the rule derived from this case would presumably apply even if the first applicant did not promptly obtain approval and begin to market, e.g., because of changes in the application that required additional review, unsatisfactory inspections, or unavailability of materials. In such cases, FDA could be barred from approving otherwise approvable subsequent ANDAs until either the first applicant eventually triggered its exclusivity with commercial marketing and the 180-day period expired, or the delisted patent expired "naturally," with the result that competition from lower priced generic drugs would be delayed.

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/s/

GARY J BUEHLER
03/26/2010